REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated March 27, 2008. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 17, 21 – 25 and 34 are under consideration in this application. Claims 1 – 16, 18-20, 26 – 33 and 35 – 41 stand canceled without prejudice or disclaimer. Claim 17 is being amended, as set forth above. These amendments are to more particularly define and distinctly claim Applicant's invention.

All the amendments to the claims are supported by the specification and no new matter is believed to have been added.

Claim Rejections - 35 USC § 112

Claims 17-25 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. To the extent that the claims are directed to a method of preventing diseases, the Examiner argues that the Applicant would need to demonstrate to the skilled artisan "that the agent would prevent any and all cases and causes of the claimed disorders." Applicant respectfully disagrees and traverse as follows.

It is unclear whether the Examiner is making a Written Description or an Enablement rejection by asserting that the Applicant must show in the specification that the "agent would prevent any and all cases and causes of the claimed disorders." As the Examiner is aware, the written description and best mode requirements are separate and distinct from the enablement requirement. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991); and MPEP Section 2161. The "written description" requirement requires the inventor to clearly convey to those skilled in the art through the specification the information that the applicant has invented as the specific subject matter of the chemical patent claims. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Although the applicant does not have to describe the subject matter claimed in the specification using exactly the same words used in the chemical patent claims, the description must be sufficiently clear to allow one of ordinary skill to recognize that the applicant invented what is claimed. *In re Lukach*, 442 F.2d 967, 969, 169 USPQ 795, 796

(CCPA 1971); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

On page 2, paragraph 2, of the Specification, Applicant stated that the Fish Protein Hydrolyzate (FPH) lowers the concentration of plasma cholesterol, homocysteine and hepatic triacylglycerols. Since elevated levels of these compounds are implicated in the various disease states, it was reasonably concluded that the FPH would have a "preventive and/or therapeutic effect" on stenosis, atherosclerosis coronary heart disease, thrombosis, myocardial infarction, stroke and fatty liver. See page 2, paragraph 2. See also page 2, paragraphs 4 and 5 and page 3, paragraphs 1 and 2.

Note particularly, as mentioned on page 3, paragraph 3, that 'hyperhomocysteine level can be established before the above indicated diseases are manifested. Since the administration of the FPH has a general homocysteine lowering effect, the FPH is **particularly suited for preventing the onset of, and lowering** the risk for the claimed diseases."

On page 5, paragraph 5 of the Specification, Applicant explicitly defined "prevention" as inviting the use of FPH prior to the onset of the condition making the compounds of the present invention eminently usable as a prophylactic agent. The Examiner is further referred to Examples 2 – 7 and Tables 1 – 3 where Applicant conclusively demonstrated the therapeutic benefits of the claimed compound and or composition.

Applicant by their disclosure and examples, have shown to a reasonable level of scientific and therapeutic certainty that their FPH have preventive and therapeutic benefits as described and claimed. The requirement that Applicant must show "that the agent would prevent any and all cases and causes of the claimed disorders," is with all due respect, unreasonable and beyond the requirements of the law. In the first place, there is no known therapeutic or preventive modality, aid, compound or composition which is 100 percent effective in 100 percent of all cases in 100 percent of the time. Even as a purely idiosyncratic matter, patients have been known to be resistant to generally accepted and well proven treatments or preventive aid but that does not invite a requirement that a specification bearing patent applications for such must show "prevention" to the unreasonable degree required by the Examiner. The science and art in this area require demonstration of efficacy to a statistically significant level and nothing more.

Moreover, it does appear to the Applicant that the Examiner is confusing the causative agent and the disease. In this particular area of practice, the presence of the

causative agent precedes the disease itself. In other words, elevated levels of cholesterol in the plasma is not co-terminus with the disease of hypercholesterolemia which is caused by elevated levels of cholesterol in the plasma. It follows therefore that decreasing the levels of the claimed compounds in the blood will prevent manifestation of the disease condition as well as being beneficial for the treatment of the disease condition. As has been adequately described and claimed, the FPH of the present invention has both a prophylactic and a treatment utility and there is no basis for maintaining the present rejection.

Moreover, to avoid the heightened "any and all cases and causes of the claimed disorders" standard imposed by the Examiner, Applicant has amended claim 17 to refer to "patients in need of such treatment" and have distinctly and precisely identified the causal nexus by limiting the claims to cases where the disease is treatable by "lowering the concentration of plasma cholesterol, homcysteine and hepatic triacylglverols. Accordingly withdrawal of this ground for rejection is respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 17, 21-25 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Kristisson & Rasco (Critical Reviews in Food Science and Nutrition, 2000, Vol. 40, No. 1, p43-81).

According to the Examiner, Kristisson and Rasco disclose administering to an animal and human, a composition comprising an enzyme treated fish protein hydrolyzate (FPH) material. In response to Applicant's arguments that Kristisson and Rasco only uses FPH in general food formulations and general antioxidant but not for treating or preventing fatty liver, hypercholesterolemia, and hyperhomocysteinemia, the Examiner stated that "a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." Applicant respectfully disagrees and now traverses as follows.

The US Code specifically provides that eligible patentable process include "a new use of a known process, machine, manufacture, composition of matter, or material." 35 U.S.C. §100. While Applicant is not necessarily admitting that the FPH of Kristisson and Rasco is qualitatively indistinguishable from that of the present invention, Applicant appreciates that for a new use of a known composition to be patentable, it must be claimed as a process, and not as a product. See *In re Thuau*, 135 F.2d 344, 57 USPQ 324 (CCPA 1943). Indeed, where an

applicant discovered a new use for an old compound, and was given a method patent for that, he was rewarded for his contributions *In re Schoenwald*, 964 F.2d 1122, 22 USPQ2d 1671 (Fed. Cir. 1992).

The claims at issue are directed to a new method or new process of treating or preventing specifically enumerated disease conditions using enzyme treated FPH; said method being both novel and unobvious and said new method being in no way anticipated by Kristisson and Rasco which did not in any way teach nor suggest any method, let alone, the use of enzyme treated FPH for prophylactic or therapeutic applications in the treatment of fatty liver, hypercholesterolemia or hyperhomocysteinemia. Accordingly, anticipation does not lie in this case and there is no basis for maintaining this ground for rejection; withdrawal of which is respectfully requested.

Rejections under 35 U.S.C. §103(a)

Claims 17, 21 – 41 stand rejected under 35 U.S.C. §103 (a) as being unpatentable over Bergeron et al. (Journal of Nutrition, 1992, Vol. 122, p 1731-1737) in view of Kristisson and Rasco (Critical Reviews in Food Science and Nutrition, 2000, Vol. 40, No. 1, p43-81) and further in view of Van Guldener and Stehouwer (Expert Opinion. Pharmacotherapy. 2001, Vol. 2, No. 9, p 1449-1460).

The Examiner asserts that Bergeron et al. teach that "fish protein has been shown to be cholesterol-lowering when fed to rabbits but hypercholesterolemic when included with a 1% corn oil diet." The Examiner admits that Bergeron et al. do not teach an enzyme treated FPH. To cure that deficiency, the Examiner asserts that Kristisson and Rasco teach an enzyme treated fish protein hydrolyzate material and that it would have been obvious to make the alleged combination to arrive at the instant invention. Applicant respectfully disagrees and now traverses as follows.

In the first place, Bergeron et al. and Kristisson and Rasco are not even properly combinable. As commonly known and described in Kristisson and Rasco (p. 44, 1st col., 4th and 5th paragraphs, *"each type of food protein has a unique molecular structure that determines its functional properties (...)"*, and *"the functional and structural properties of food proteins thus vary tremendously (..)"*. Moreover, *"enzymatic hydrolysis of fish proteins generates a mixture of free amino acids, di-, tri-, and oligopeptides, increases the number of polar groups and the solubility of the hydrolyzate, and therefore modifies functional characteristics of the proteins, improving their functional characteristics and bioavailability. The choice of substrate and proteases employed and the degree to which the protein is hydrolyzed affect the*

physicochemical properties of the resulting hydrolyzate (p. 64, 2nd col., 1st paragraph)." To that extent, a deficiency in a prior art teaching the use of fish protein cannot simply be cured by combination a prior art teaching the use of enzyme digested fish protein hydrolyzate, seeing as above, they are, in fact, markedly different pharmacologically speaking.

Whereas Bergeron et al. conclude from their experiments that "current data indicates that fish protein can produce variable effects on serum total cholesterol concentrations depending in part on the amount and origin of the dietary lipid with which it is combined," nothing in Bergeron nor the asserted combination suggests, teaches nor would otherwise make it obvious to use fish protein uncombined with dietary lipid for prophylactic or therapeutic uses in the treatment or prevention of fatty liver, hypercholesterolemia or hyperhomocysteinemia. In particularly, Bergeron et al. teach variable and indeterminate effect of fish protein combined with dietary lipid on serum total cholesterol and do not teach the cardioprotective effect, if any, of fish protein hydrolyzate.

As motivation for using Kristisson and Rasco to cure the deficiencies in Bergeron, the Examiner asserts that one of skill in the art would have tried to combine the cholesterol lowering effect of fish protein diet as taught by Bergeron et al., with the ability to obtain fish protein hydrolyzate with low lipid content, and therefore to lower the risk of cardiovascular diseases.

Not only are the two references not combinable, as mentioned above, in the sense that one teaches the use of fish protein and the other teaches the use of fish protein hydrolyzate (both compositions having been explicitly taught by Kristisson to be chemically, biochemically and functionally distinct), the combined art fails to teach the prophylactic and/or therapeutic use of fish protein hydrolyzate as a hepatoprotective and cardioprotective substance. If anything, it is generally known that fish oil found in fish fillets is universally rich in omega 3 fatty acids and is cardioprotective making it counterintuitive for cardio-prophylactic and cardiotherapeutic uses to attempt to use enzymatic hydrolyzates of fish protein for the claimed uses since that process would have the effect of substantially stripping the fish protein of supposedly beneficial omega 3 fatty acids. That such hydrolyzate would have the effect shown and claimed in the instant invention, despite being substantially stripped of omega-3-fatty acids, is totally unexpected. See page 15 of the Specification. Such unexpected and unobvious effect could not have been cured by Kristisson and Rasco which did not teach nor suggest any clinical use for FPH nor by Bergeron which was concerned with the beneficial uses of fish protein combined with dietary lipids. Assuming for the sake of argument, that despite being biochemically and pharmacologically distinct, the Examiner insists that fish protein and FPH would function in substantially the same way, it cannot also be held judging from the remarkable disclosed in the specification that their pharmacologic action in terms of treating the claimed disease condition is

substantially similar.

The Examiner is reminded that impermissible hindsight precludes the use of the novel medical uses of this invention to deny patentability to the same invention that informed the hindsight. Nor is this the "obvious to try" situation contemplated by the Supreme Court in KSR because Bergeron's fish protein/dietary lipid is a far cry from enzymatic fish protein hydrolyzate being used for prophylactic and/or therapeutic applications for fatty liver, hypercholesterolemia and hyperhomocysteinemia. As evidence that the Examiner is resorting to impressible hindsight, the Examiner asserts that it was always known that elevated homocysteine levels in blood caused atherosclerotic disease. While Applicant is not contending that, Applicant is merely claiming that because it was unexpected and unobvious, to attain the results disclosed, that they deserve to be rewarded for their contribution to the pharmaceutical arts, no more and no less, for discovering that fish protein hydrolyzate can be used to treat or prevent hyperhomocysteinemia, fatty liver, and hypercholesterolemia.

In fact, Bergeron suggests that the lipoprotein lipase (LPL) activity is a determinant for the fish-protein induced decrement of in VLDL triglycerides and concomitant rise in HDL cholesterol in rabbits (p. 1736, 2nd col., 2nd paragraph). Bergeron further discusses that a fish protein induced rise in lipoprotein lipase activity may result from an increase in the concentration of apo C-II as cofactor, which is considered important for full activity expression of the LPL. One skilled in the art who is familiar with mechanism for enzymatic reactions would not assume that Bergeron's unhydrolysed proteins would have the same effect as a fish protein hydrolyzate on an enzymatic reaction, even if they came from the same origin/fish. As demonstrated by Example 4 ([0059]-[0061]) in the specification of the present invention, the administration of FPH to rats inhibits the Acyl-CoA:cholesterol transferase (ACAT) to 0.035 nmol/mg/min, which catalyses the reaction in which fatty acyl-CoA is esterified to cholesterol, while unhydrolysed proteins (i.e., casein) only inhibits the ACAT to 0.05 nmol/mg/min. As such, unhydrolyzed protein does not necessarily deliver the same mechanism and as significant beneficial effect on cholesterol as FPH (Fig. 3).

For at least the fact that the asserted combination is not only improper but fails to teach all the elements of the instant invention, and for at least the fact that the results obtained and disclosed in the invention are unexpected and unobvious to try, Applicant respectfully requests that the Examiner reconsider and withdraw this grounds for rejection.

Regarding the rejection of claims 26 – 41 under 35 U.S.C. § 103(a), said rejection is now moot in view of the cancellation of said claims without prejudice or disclaimer.

Conclusion

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicant respectfully contends that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicant's undersigned representative at the address and phone number indicated below.

Respectfully submitted,

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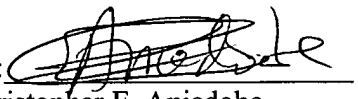
By: 
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